

## PATENT COOPERATION TREATY

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## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

REC'D 02 AUG 2005

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Applicant's or agent's file reference P-INCI-X-04-0278		<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)	
International application No. PCT/EP2004/008515		International filing date (day/month/year) 29.07.2004	Priority date (day/month/year) 30.07.2003
International Patent Classification (IPC) or both national classification and IPC A61K31/536, A61K31/404, A61K31/4045			
Applicant LABORATORIOS DEL DR. ESTEVE S.A. et al.			
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 4 sheets, including this cover sheet.</p> <p><input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of 25 sheets.</p>			
<p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the opinion</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p>			
Date of submission of the demand  28.02.2005		Date of completion of this report  29.07.2005	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized Officer  Economou, D  Telephone No. +49 89 2399-8599 	

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP2004/008515

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, Pages**

1-421 as originally filed

**Claims, Numbers**

42-45 as originally filed

1-41 received on 02.06.2005 with letter of 30.05.2005

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).  
☐ the language of publication of the international application (under Rule 48.3(b)).  
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.  
☐ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority in written form.  
☐ furnished subsequently to this Authority in computer readable form.  
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.  
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. **PCT/EP2004/008515**

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**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Yes: Claims	1-41
	No: Claims	
Inventive step (IS)	Yes: Claims	1-41
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-41
	No: Claims	

**2. Citations and explanations**

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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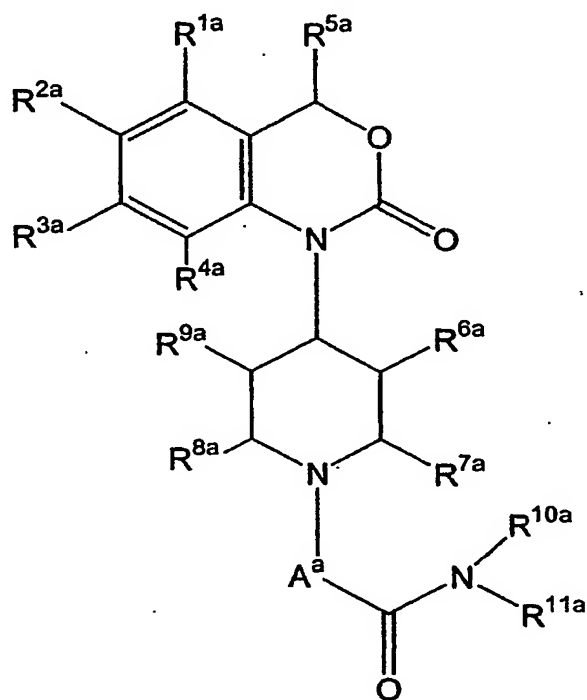
International application No. PCT/EP2004/008515

- 1). The subject-matter of claims 1-41 fulfils the requirements of industrial applicability.
- 2). Combinations comprising as compound (A) a compound of formula (Ia) combined with compounds (Ib)-(Ih) are novel and inventive since compounds of formula (Ia) appear to be novel and not obvious from the available prior art. Hence, the subject-matter of claims 1-41 is novel and involves also an inventive step since it is not obvious from the available prior art.

# Claims

1. An active substance combination, characterized in that it comprises:

(A) at least one compound with neuropeptide Y (NPY) -receptor affinity, selected from the group consisting of compounds of general formula (Ia),



(Ia)

wherein

$R^{1a}$ ,  $R^{2a}$ ,  $R^{3a}$ ,  $R^{4a}$  are each independently selected from the group consisting of hydrogen, halogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system, an optionally at least mono-substituted aryl- or heteroaryl radical,

which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ringsystem, a nitro, cyano,  $-OR^{12a}$ ,  $-OC(=O)R^{13a}$ ,  $-SR^{14a}$ ,  $-SOR^{14a}$ ,  $-SO_2R^{14a}$ ,  $-NH-SO_2R^{14a}$ ,  $-SO_2NH_2$  and  $-NR^{15a}R^{16a}$  moiety,

$R^{5a}$  represents hydrogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical or a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical,

$R^{6a}$ ,  $R^{7a}$ ,  $R^{8a}$ ,  $R^{9a}$  are each independently selected from the group consisting of hydrogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical, a cyano and a  $COOR^{17a}$  moiety,

$A^a$  represents a bridge member  $-CHR^{18a}-$  or  $-CHR^{18a}-CH_2-$ ,

$R^{10a}$  represents hydrogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical or an optionally at least mono-substituted aryl- or heteroaryl radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system,

$R^{11a}$  represents an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ringsystem, or an optionally at least mono substituted aryl- or heteroaryl radical, which may be bonded via an optionally at least mono-substituted

alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ringsystem, or

5  $R^{10a}$  and  $R^{11a}$  together with the bridging nitrogen atom form an optionally at least mono-substituted, saturated, unsaturated or aromatic heterocyclic ring that may contain at least one further heteroatom as a ring member and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ringsystem,

10  $R^{12a}$  represents hydrogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system, or an optionally at least mono-substituted aryl- or heteroaryl radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system,

20  $R^{13a}$  represents hydrogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system, or an optionally at least mono-substituted aryl- or heteroaryl radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system,

30  $R^{14a}$  represents an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one

heteroatom as ring member containing cycloaliphatic radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system, or an optionally at least mono-substituted aryl- or heteroaryl radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system,

$R^{15a}$  and  $R^{16a}$  each are independently selected from the group consisting of hydrogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system, or an optionally at least mono-substituted aryl- or heteroaryl radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system,

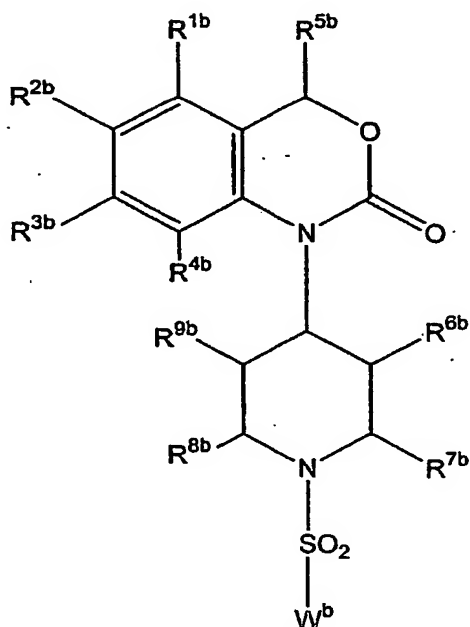
or  $R^{15a}$  and  $R^{16a}$  together with the bridging nitrogen atom form a saturated, unsaturated or aromatic heterocyclic ring, which may be at least mono-substituted and/or contain at least one further heteroatom as a ring member,

$R^{17a}$  represents hydrogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical or an optionally at least mono-substituted aryl- or heteroaryl radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system,

$R^{18a}$  represents hydrogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical or an optionally at least mono-substituted aryl- or heteroaryl radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system,

optionally in form of one of its stereoisomers, preferably enantiomers or diastereomers, its racemate or in form of a mixture of at least two of its stereoisomers, preferably enantiomers or diastereomers, in any mixing ratio, or a physiologically acceptable salt thereof, or a solvate, respectively, and

(B) at least one compound with 5-HT<sub>6</sub> receptor affinity selected from the group consisting of the benzoxazinone-derived sulfonamide compounds of general formula (Ib)



(Ib)

wherein

$R^{1b}$ ,  $R^{2b}$ ,  $R^{3b}$ ,  $R^{4b}$  are each independently selected from the group consisting of hydrogen, halogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system, an optionally at least mono-substituted aryl- or heteroaryl radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ringsystem, a nitro, cyano,  $-OR^{10b}$ ,  $-O(C=O)R^{11b}$ ,  $-(C=O)OR^{11b}$ ,  $-SR^{12b}$ ,  $-SOR^{12b}$ ,  $-SO_2R^{12b}$ ,  $-NH-SO_2R^{12b}$ ,  $-SO_2NH_2$  and a  $-NR^{13b}R^{14b}$  moiety,

$R^{5b}$  represents hydrogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical or a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical,

$R^{6b}$ ,  $R^{7b}$ ,  $R^{8b}$ ,  $R^{9b}$  are each independently selected from the group consisting of hydrogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical, a cyano group and a  $COOR^{15b}$  moiety,

$W^b$  represents an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical,

a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical, which may be bonded via an optionally mono-substituted alkylene group and/or may

be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system,

an optionally at least mono-substituted aryl or heteroaryl radical, which may be bonded via an optionally at least mono-substituted alkylene or alkenylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system,

a  $\text{NR}^{16b}\text{R}^{17b}$ -moiety, or

a  $\text{COR}^{18b}$ -moiety,

$\text{R}^{10b}$  represents hydrogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system, or an optionally at least mono-substituted aryl- or heteroaryl radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system,

$\text{R}^{11b}$  represents hydrogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system, or an optionally at least mono-substituted aryl- or heteroaryl radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system,

$R^{12b}$  represents an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system, or an optionally at least mono-substituted aryl- or heteroaryl radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system,

$R^{13b}$  and  $R^{14b}$  each are independently selected from the group consisting of hydrogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system, or an optionally at least mono-substituted aryl- or heteroaryl radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system,

or  $R^{13b}$  and  $R^{14b}$  together with the bridging nitrogen atom form a saturated, unsaturated or aromatic heterocyclic ring, which may be at least mono-substituted and/or contain at least one further heteroatom as a ring member,

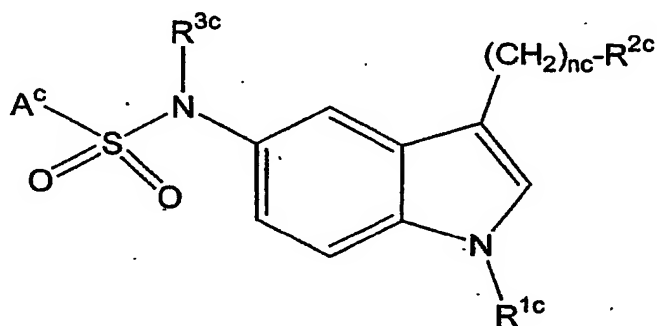
$R^{15b}$  represents hydrogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical or an optionally at least mono-substituted aryl- or heteroaryl radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system,

$R^{16b}$  represents an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical,

$R^{17b}$  represents an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, and

$R^{18}$  represents an optionally at least mono-substituted aryl radical

optionally in form of one of its stereoisomers, preferably enantiomers or diastereomers, its racemate or in form of a mixture of at least two of its stereoisomers, preferably enantiomers or diastereomers, in any mixing ratio, or a physiologically acceptable salt thereof, or a solvate, respectively, and compounds derived from sulfonamide of general formula (Ic),



(Ic)

wherein

$R^{1c}$  represents hydrogen, an optionally at least mono-substituted, linear or branched alkyl radical, an optionally at least mono-substituted phenyl radical or an optionally at least mono-substituted benzyl radical,

$R^{2c}$  represents a  $-NR^{4c}R^{5c}$  moiety or a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical, which may be condensed with a saturated or

unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing mono- or bicyclic cycloaliphatic ringsystem,

5  $R^{3c}$  represents hydrogen or an optionally at least mono- substituted, linear or branched alkyl radical,

$R^{4c}$  and  $R^{5c}$ , identical or different, represent hydrogen or an optionally at least mono-substituted, linear or branched alkyl radical, or

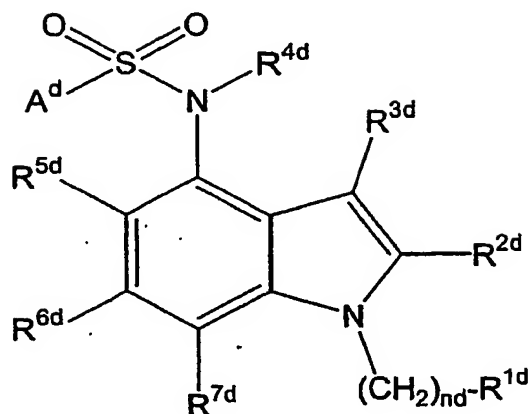
10  $R^{4c}$  and  $R^{5c}$  together with the bridging nitrogen atom form an optionally at least mono-substituted, saturated or unsaturated heterocyclic ring, which may contain at least one further heteroatom as a ring member and/or may be condensed with a saturated or unsaturated, optionally at least mono-  
15 substituted, optionally at least one heteroatom as ring member containing mono- or bicyclic cycloaliphatic ringsystem,

$A^c$  represents an optionally at least mono-substituted mono- or polycyclic aromatic ringsystem, which may be bonded via an optionally at least mono-  
20 substituted alkylene-, an optionally at least mono-substituted alkenylene- or an optionally at least mono-substituted alkynylene group and/or may contain at least one heteroatom as a ring member in one or more of its rings,

nc represents 0, 1, 2, 3 or 4;

25 optionally in form of one of its stereoisomers, preferably enantiomers or diastereomers, its racemate or in form of a mixture of at least two of its stereoisomers, preferably enantiomers or diastereomers, in any mixing ratio, or a corresponding physiologically acceptable salt or a corresponding solvate,

30 and compounds of the general formula (Id)



(Id)

5  $R^{1d}$  represents a  $-NR^{8d}R^{9d}$  radical or a saturated or unsaturated, optionally at least mono-substituted cycloaliphatic radical, which may contain at least one heteroatom as a ring member and/or which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system,

10  $R^{2d}$ ,  $R^{3d}$ ,  $R^{5d}$ ,  $R^{6d}$  and  $R^{7d}$ , identical or different, each represent hydrogen, halogen, nitro, alkoxy, cyano, a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical, or an optionally at least mono-substituted phenyl or heteroaryl radical,

15  $R^{4d}$  is hydrogen or a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical,

20  $R^{8d}$  and  $R^{9d}$ , identical or different, each represent hydrogen or a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical,

or

$R^{8d}$  and  $R^{9d}$  together with bridging nitrogen atom form a saturated or unsaturated, optionally at least mono-substituted heterocyclic ring, which may contain at least one additional heteroatom as a ring member and/or may be condensed with a saturated or unsaturated, optionally at least mono-substituted mono- or bicyclic cycloaliphatic ring system, which may optionally contain at least one heteroatom as a ring member,

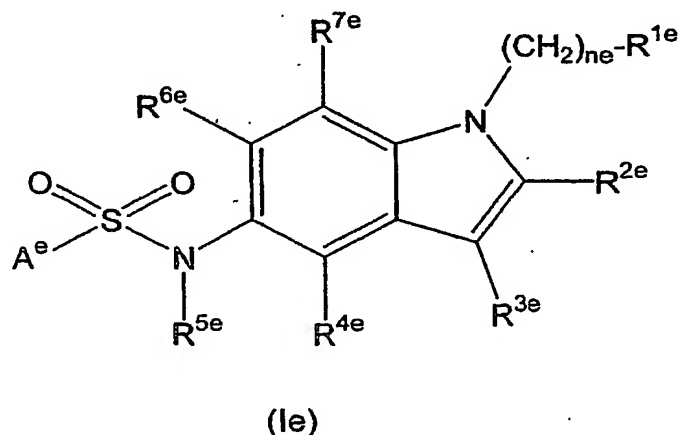
$A^d$  represents an optionally at least mono-substituted mono- or polycyclic aromatic ring system, which may be bonded via an optionally at least mono-substituted alkylene, alkenylene or alkynylene group and/or which may contain at least one heteroatom as a ring member in one or more of its rings,

and

$n$  is 0, 1, 2, 3 or 4;

optionally in form of one of its stereoisomers, preferably enantiomers or diastereomers, its racemate or in form of a mixture of at least two of its stereoisomers, preferably enantiomers or diastereomers, in any mixing ratio, or a salt thereof, preferably a corresponding, physiologically acceptable salt thereof, or a corresponding solvate thereof,

and sulphonamide-derived compounds of general formula (Ie),



wherein

$R^{1e}$  represents a  $-NR^{8e}R^{9e}$  radical or a saturated or unsaturated, optionally at least mono-substituted cycloaliphatic radical, which may optionally contain at least one heteroatom as a ring member and/or which may be condensed with a saturated or unsaturated, optionally at least mono-substituted mono- or bicyclic cycloaliphatic ring system, which may optionally contain at least one heteroatom as a ring member,

$R^{2e}$ ,  $R^{3e}$ ,  $R^{4e}$ ,  $R^{6e}$  and  $R^{7e}$ , identical or different, each represent hydrogen, halogen, nitro, alkoxy, cyano, a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical or an optionally at least mono-substituted phenyl or an optionally at least mono-substituted heteroaryl radical,

$R^{5e}$  represents hydrogen or a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical,

$R^{8e}$  and  $R^{9e}$ , identical or different, each represent hydrogen or a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical,

or

$R^{8e}$  and  $R^{9e}$  together with the bridging nitrogen atom form a saturated or unsaturated, optionally at least mono-substituted heterocyclic ring, which may contain at least one additional heteroatom as a ring member and/or which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, mono- or bicyclic cycloaliphatic ring system which may optionally contain at least one heteroatom as a ring member,

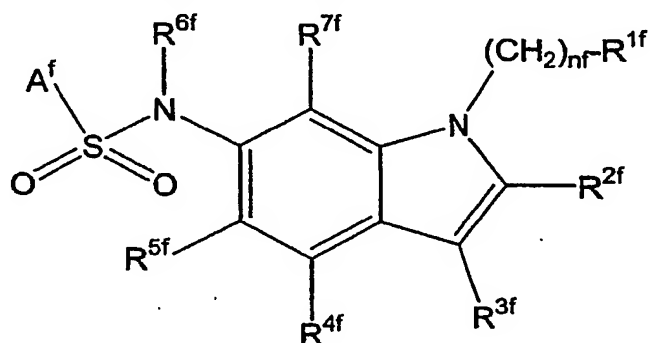
$A^e$  represents an optionally at least mono-substituted mono- or polycyclic aromatic ring system, which may be bonded via an optionally at least mono-substituted alkylene, alkenylene or alkynylene group and/or which may contain at least one heteroatom as a ring member in one or more of its rings

and

ne is 0, 1, 2, 3 or 4;

optionally in the form of one of its stereoisomers, preferably enantiomers or diastereomers, its racemate or in the form of a mixture of at least two of its stereoisomers, preferably enantiomers or diastereomers, at any mixture ratio, or a corresponding, physiologically acceptable salt, or a corresponding solvate

and sulphonamide-derived compounds of general formula (If),



(If)

wherein

R<sup>1f</sup> represents a -NR<sup>8f</sup>R<sup>9f</sup> radical or a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing cycloaliphatic radical, which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system,

R<sup>2f</sup>, R<sup>3f</sup>, R<sup>4f</sup>, R<sup>5f</sup> and R<sup>7f</sup>, identical or different, each represent hydrogen, halogen, nitro, alkoxy, cyano, a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical, or an optionally at least mono-substituted phenyl or optionally at least mono-substituted heteroaryl radical,

$R^{6f}$  represents hydrogen or a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical,

$R^{8f}$  and  $R^{9f}$ , identical or different, each represent hydrogen or a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical,

or

$R^{8f}$  and  $R^{9f}$ , together with the bridging nitrogen atom, form a saturated or unsaturated, optionally at least mono-substituted heterocyclic ring, which may contain at least one further heteroatom as a ring member and/or which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system,

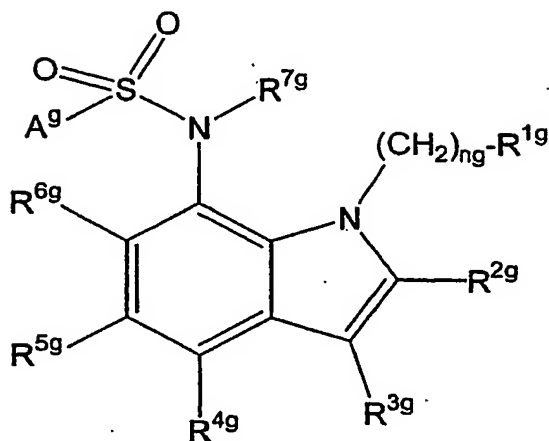
$A^f$  represents an optionally at least mono-substituted mono- or polycyclic aromatic ring system, which may be bonded via an optionally at least mono-substituted alkylene, alkenylene or alkynylene group and/or which may contain at least one heteroatom as a ring member in one or more of its rings,

and

$n_f$  is 0, 1, 2, 3 or 4;

optionally in the form of one of its stereoisomers, preferably enantiomers or diastereomers, its racemate or in the form of a mixture of at least two of its stereoisomers, preferably enantiomers or diastereomers, at any mixture ratio, or a corresponding, physiologically acceptable salt, or a corresponding solvate

and sulphonamide-derived compounds of general formula (Ig).



(Ig)

wherein

R<sup>1g</sup> is a -NR<sup>8g</sup>R<sup>9g</sup> radical or a saturated or unsaturated, optionally at least mono-substituted cycloaliphatic radical, which may optionally contain at least one heteroatom as a ring member and which may be condensed with a saturated or unsaturated, optionally at least mono-substituted mono- or bicyclic cycloaliphatic ring system which may optionally contain at least one heteroatom as a ring member,

R<sup>2g</sup>, R<sup>3g</sup>, R<sup>4g</sup>, R<sup>5g</sup> and R<sup>6g</sup>, identical or different, each represent hydrogen, halogen, nitro, alkoxy, cyano, a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical, or an optionally at least mono-substituted phenyl radical or an optionally at least mono-substituted heteroaryl radical,

R<sup>7g</sup> represents hydrogen or a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical,

R<sup>8g</sup> and R<sup>9g</sup>, identical or different, represent hydrogen or a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical,

or

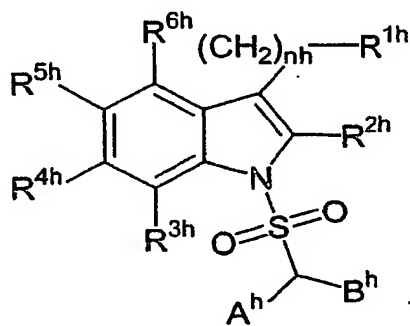
$R^{8g}$  and  $R^{9g}$  together with the bridging nitrogen atom form a saturated or unsaturated, optionally at least mono-substituted heterocyclic ring, which may contain at least one additional heteroatom as a ring member and/or which may be condensed with a saturated or unsaturated, optionally at least mono-substituted mono- or bicyclic cycloaliphatic ring system, which may optionally contain at least one heteroatom as a ring member,

$A^9$  represents an optionally at least mono-substituted mono- or polycyclic aromatic ring system, which may be bonded via an optionally at least mono-substituted alkylene, alkenylene or alkynylene group and/or which may contain at least one heteroatom as a ring member in one or more of its rings,

$n_g$  is 0, 1, 2, 3 or 4;

optionally in the form of one of its stereoisomers, preferably enantiomers or diastereomers, its racemate or in the form of a mixture of at least two of its stereoisomers, preferably enantiomers or diastereomers, at any mixture ratio, or a corresponding, physiologically acceptable salt, or a corresponding solvate,

and sulphonamide-derived compounds of general formula (Ih)



(Ih)

wherein

5  $R^{1h}$  represents a  $-NR^{7h}R^{8h}$  radical or a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing cycloaliphatic radical, which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system,

15  $R^{2h}$ ,  $R^{3h}$ ,  $R^{4h}$ ,  $R^{5h}$  and  $R^{6h}$ , identical or different, each represent hydrogen, halogen, cyano, nitro, a saturated or unsaturated, linear or branched aliphatic radical, a linear or branched alkoxy radical, a linear or branched alkylthio radical, hydroxy, trifluoromethyl, a saturated or unsaturated cycloaliphatic radical, an alkylcarbonyl radical, a phenylcarbonyl or a  $-NR^{9h}R^{10h}$  group,

20  $R^{7h}$  and  $R^{8h}$ , identical or different, each represent hydrogen or a saturated or unsaturated, optionally at least mono-substituted linear or branched aliphatic radical,

or

25  $R^{7h}$  and  $R^{8h}$ , together with the bridging nitrogen atom form a saturated or unsaturated, optionally at least mono-substituted, optionally at least one further heteroatom as a ring member containing heterocyclic ring which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system,

30  $R^{9h}$  and  $R^{10h}$ , identical or different, each represent hydrogen or a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical,

or

5  $R^{9h}$  and  $R^{10h}$ , together with the bridging nitrogen atom form a saturated or unsaturated, optionally at least mono-substituted, optionally at least one further heteroatom as a ring member containing heterocyclic ring which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system,

10  $A^h$  and  $B^h$ , identical or different, each represent a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical

or

15  $A^h$  and  $B^h$ , together with the carbon atom to which they are bonded, form a saturated or unsaturated, but not aromatic, optionally at least mono-substituted cycloalkyl ring,

20 and

$nh$  is 0, 1, 2, 3, or 4,

25 optionally in form of one of their stereoisomers, preferably enantiomers or diastereomers, their racemate or in form of a mixture of at least two of their stereoisomers, preferably enantiomers or diastereomers, in any mixing ratio, or a salt thereof, preferably a corresponding physiologically acceptable salt thereof or a corresponding solvate thereof.

- 30 2. The combination according to claim 1, characterized in that it comprises 1-99% by weight of component (A) and 99-1% by weight of component (B), more preferably 10-80% by weight of component (A) and 90-20% by weight of component (B), referring those percentages to the total weight of both components (A) and (B).

3. A medicament comprising an active substance combination according to any one of the claims 1 or 2 and optionally one or more pharmacologically acceptable adjuvants.

4. A medicament according to claim 3 for regulation of appetite, for maintenance, increase or reduction of body weight, for prophylaxis and/or treatment of disorders related to food ingestion, preferably for prophylaxis and/or treatment of obesity, anorexia, cachexia, bulimia, diabetes, preferably type II diabetes (non-insulin-dependent diabetes mellitus), or for prophylaxis and/or treatment of gastrointestinal tract disorders, preferably of the irritable bowel syndrome, for prophylaxis and/or treatment of Peripheral Nervous System Disorders, Central Nervous System Disorders, arthritis, epilepsy, anxiety, panic, depression, cognitive disorders, memory disorders, cardiovascular diseases, senile dementia processes, such as Alzheimer's, Parkinson's and/or Huntington's Disease, schizophrenia, psychosis, infantile hyperkinesia (ADHD, attention deficit / hyperactivity disorder), pain, hypertensive syndrome, inflammatory diseases, immunologic diseases or for improvement of cognition.

5. Use of the combination according to any one of claims 1 or 2, for the manufacture of a medicament for regulation of appetite.

6. Use of the combination according to any one of claims 1 or 2, for the manufacture of a medicament for maintenance, increase or reduction of body weight.

7. Use of the combination according to any one of claims 1 or 2, for the manufacture of a medicament for prophylaxis and/or treatment of disorders related to food ingestion, preferably for prophylaxis and/or treatment of obesity, anorexia, cachexia, bulimia, diabetes, preferably type II diabetes (non-insulin-dependent diabetes mellitus).

8. Use of the combination according to any one of claims 1 or 2, for the manufacture of a medicament for prophylaxis and/or treatment of gastrointestinal tract disorders, preferably of the irritable bowel syndrome.
- 5 9. Use of the combination according to any one of claims 1 or 2, for the manufacture of a medicament for prophylaxis and/or treatment of Peripheral Nervous System Disorders.
- 10 10. Use of the combination according to any one of claims 1 or 2, for the manufacture of a medicament for prophylaxis and/or treatment of Central Nervous System Disorders.
11. Use of the combination according to any one of claims 1 or 2, for the manufacture of a medicament for prophylaxis and/or treatment arthritis.
- 15 12. Use of the combination according to any one of claims 1 or 2, for the manufacture of a medicament for prophylaxis and/or treatment of epilepsy.
- 20 13. Use of the combination according to any one of claims 1 or 2, for the manufacture of a medicament for prophylaxis and/or treatment of anxiety.
14. Use of the combination according to any one of claims 1 or 2 for the manufacture of a medicament for prophylaxis and/or treatment of panic.
- 25 15. Use of the combination according to any one of claims 1 or 2, for the manufacture of a medicament for prophylaxis and/or treatment of depression.
16. Use of the combination according to any one of claims 1 or 2, for the manufacture of a medicament for prophylaxis and/or treatment of bipolar disorders.
- 30 17. Use of the combination according to any one of claims 1 or 2, for the manufacture of a medicament for prophylaxis and/or treatment of cognitive disorders.

18. Use of the combination according to any one of claims 1 or 2, for the manufacture of a medicament for prophylaxis and/or treatment of memory disorders.
- 5
19. Use of the combination according to any one of claims 1 or 2, for the manufacture of a medicament for prophylaxis and/or treatment of cardiovascular diseases.
- 10
20. Use of the combination according to any one of claims 1 or 2, for the manufacture of a medicament for prophylaxis and/or treatment of senile dementia processes.
- 15
21. Use of the combination according to any one of claims 1 or 2, for the manufacture of a medicament for prophylaxis and/or treatment of neurodegenerative diseases, preferably Parkinson's disease, Alzheimer's disease, Huntington's disease and Multiple Sklerosis.
- 20
22. Use of the combination according to any one of claims 1 or 2, for the manufacture of a medicament for prophylaxis and/or treatment of schizophrenia.
- 25
23. Use of the combination according to any one of claims 1 or 2, for the manufacture of a medicament for prophylaxis and/or treatment of psychosis.
24. Use of the combination according to any one of claims 1 or 2, for the manufacture of a medicament for prophylaxis and/or treatment of infantile hyperkinesia (ADHD, attention deficit / hyperactivity disorder).
- 30
25. Use of the combination according to any one of claims 1 or 2, for the manufacture of a medicament for prophylaxis and/or treatment of pain.

26. Use of the combination according to any one of claims 1 or 2, for the manufacture of a medicament for prophylaxis and/or treatment of hypertensive syndrome.
- 5 27. Use of the combination according to any one of claims 1 or 2, for the manufacture of a medicament for prophylaxis and/or treatment of inflammatoric diseases.
- 10 28. Use of the combination according to any one of claims 1 or 2, for the manufacture of a medicament for prophylaxis and/or treatment of immunologic diseases.
29. Use of the combination according to any one of claims 1 or 2, for the manufacture of a medicament for improvement of cognition.
- 15 30. A pharmaceutical formulation, characterized in that it comprises an active substance combination according to any one of claims 1 or 2 and optionally one or more pharmacologically acceptable adjuvants.
- 20 31. The pharmaceutical formulation according to claim 30, characterized in that it is present in solid pharmaceutical forms such as tablets, tablets, chewing tablets, chewing gums, dragées, capsules, suppositories, powder preparations, transdermal therapeutic systems, transmucosal therapeutic systems, or in liquid and semi-liquid pharmaceutical forms such as drops or
- 25 such as juice, sirup, solution, emulsion, suspension, preferably in form of tablets, capsules, drops or solution.
32. The pharmaceutical formulation according to claim 30, characterized in that it is present in form of of multiple particles, preferably microtablets,
- 30 microcapsules, microspheroids, granules, crystals or pellets, optionally compacted in a tablet, filled in a capsule or suspended in a suitable liquid.

33. The pharmaceutical formulation according to one or more of claims 30-32, characterized in that it is for oral, intravenous, intramuscular, subcutaneous, intrathecal, epidural, buccal, sublingual, pulmonal, rectal, transdermal, nasal or intracerebroventricular application, preferably oral or intravenous.
- 5 34. The pharmaceutical formulation according to one or more of claims 30-33, characterized in that at least one of the components of the active substance combination (A) or (B) is present at least partially in sustained-release form.
- 10 35. The pharmaceutical formulation according to claim 34, characterized in that the medicament has at least one coating or one matrix comprising at least one material, which sustains active substance release.
- 15 36. The pharmaceutical formulation according to claim 35, characterized in that the sustained-release material is based on optionally modified, water-insoluble, natural, semisynthetic or synthetic polymer, or a natural wax or fat or fatty alcohol or semisynthetic or synthetic fatty acid, or on a mixture of at least two of these afore mentioned components.
- 20 37. The pharmaceutical formulation according to claim 36, characterized in that the water-insoluble polymer is based on an acrylic resin, which is preferably selected from the group of poly(meth)acrylates, poly(C<sub>1-4</sub>)dialkylamino(C<sub>1-4</sub>)alkyl (meth)acrylates and/or copolymers thereof or a mixture of at least two of the afore-mentioned polymers.
- 25 38. The pharmaceutical formulation according to claim 36, characterized in that the water-insoluble polymers are cellulose derivatives, preferably alkyl cellulose and even more preferably ethyl cellulose, or cellulose esters.
- 30 39. The pharmaceutical formulation according to claim 36, characterized in that the wax is carnauba wax, beeswax, glycerol monostearate, glycerol monobehenate, glycerol ditripalmitostearate, microcrystalline wax or a mixture of at least two of these components.

40. The pharmaceutical formulation according to one or more of claims 36 to 39, characterized in that polymers have been used in combination with one or more plasticizers.
- 5 41. The pharmaceutical formulation according to one or more of claims 30 to 40, characterized in that besides the sustained-release form, at least one of the active substance components (A) or (B) is present in a non-sustained-release form.